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EXAMINER	
LEE, JAE W	
ART UNIT	**PAPER NUMBER**
1656	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/29/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/817,204	AYAD ET AL.	
	Examiner	Art Unit	
	Jae W. Lee	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 April 2004*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-51* is/are pending in the application.

4a) Of the above claim(s) *14-25 and 27-51* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-13 and 26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application status

Claims 1-51 are pending in this application.

Preliminary amendments for claims, filed on 08/30/2006, are acknowledged.

Priority

A claim of priority to the U.S. Provisional Application 60/459,788, filed on 04/02/2003, is acknowledged.

Election

Applicant's election with traverse of Group I, Claims 1, 3-13 and 26 with SEQ ID NOs: 2 and 5, is acknowledged. The traversal is on the ground(s) that claim 2 has been amended to clarify it is drawn to the isolated nucleic acid molecule that encodes the polypeptide of claim 1. Upon further consideration, Applicant's argument is found persuasive and Claim 2 is rejoined with Group I.

Second traversal is on the ground(s) that there would be no serious burden on the Examiner to examine SEQ ID NOs:1-6 together because polynucleotides encoding Tome-1 proteins are *structurally and functionally related.* Although Applicants allege that SEQ ID NOs: 1-3 are structurally related as shown in Figure 1 of the specification, it is stated in the specification on pg. 61 line 9, that "*Xenopus* Tome-1 was determined to be 30% identical to human Tome-1," which supports the notion of their structure

dissimilarities. Even if the proteins were structurally and functionally related as Applicants allege, the subject matter of elected Group I is directed to an isolated nucleic acid molecules and not proteins or amino acid sequences, thus, the Applicant's argument is not found persuasive. In addition, where structural identity is required, such as for hybridization or expression, the different sequences have different effects. Thus, the restriction requirement is still deemed proper, and is therefore made FINAL.

Claims 1-13 and 26 will be examined on the merits. Claims 14-25 and 27-51 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Objections to the Specification

The specification is objected to because the title is contains a word such as "Novel". The words "new," "improved," "improvement of," and "improvement in" are not considered as part of the title of an invention, these words should not be included at the beginning of the title of the invention (see M.P.E.P. 606)

Appropriate correction for each error is required.

Claim Objections

Claims 1-3 (4-13 and 26 dependent therefrom) are objected to because the recitation of "Tome-1," " SCF," or "wee1"should be in parenthesis and follow the phrase it abbreviates when used for the first time.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 7-13 and 26 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 (7, 8, 10-13 and 26 dependent therefrom) and 2 recite the phrase, "Tome-1," which is unclear. It is not clear with respect to what Applicants intend as being encompassed by Tome-1. In the interest of advancing prosecution, Tome-1 is interpreted to be any protein that comprises a destruction box, F box, a KEN sequence or an activity that modulates mitotic entry, based on pg. 15, line 21 through pg. 16, line 11.

Claims 1 (7, 8, 10-13 and 26 dependent therefrom) and 2 recite the phrase, "Tome-1 activities," or "an SCF complex component activity," which is unclear because an activity of a protein may encompass a variety of different biological activities. These

include but are not limited to immunological activity, such as acting as an antigen for an antibody; regulatory activity, such as that exhibited by many proteins which control transcription and/or translation of not only their encoding nucleic acids but other nucleic acids as well; or enzymatic activity, for example, phosphorylated-Wee1 binding activity. It is not clear what is encompassed by the "activities" or "activity" of Tome-1 or an SCF complex component, and if it includes biological activities in addition to enzymatic activity. In the interest of advancing prosecution, it is interpreted to be any activity exerted by a Tome-1 protein.

Claim 2 recites the limitation "the polypeptide" in Claim 1. There is insufficient antecedent basis for this limitation in the claim because the subject matter of Claim 1 is drawn to an isolated nucleic acid molecule, and not to a polypeptide.

Claim 2 recites the phrase, "wee1," which is unclear. It is not clear with respect to what Applicants intend as being encompassed by "wee1."

Claim 2 recites the phrase, "an SCF complex component," which is unclear. It is not clear with respect to what Applicants intend as being encompassed by "an SCF complex component."

Claim 3 recites the phrase, "the nucleic acid molecule encodes a nucleotide sequence," which is unclear. Nucleic acid molecules cannot encode a nucleotide sequence. In the interest of advancing prosecution, it is interpreted to be, "the nucleic acid molecule encodes a polypeptide sequence."

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-13 and 26 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-13 and 26 are directed to any isolated nucleic acid molecule which encodes any polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2, wherein the polypeptide has one or more Tome-1 activities.

To satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus of [compositions or methods], it must be clear that: (1) the identifying characteristics of the claimed [compositions or methods] have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed.

The specification discloses a single example of an isolated nucleic acid molecule from *Xenopus laevis* consisting of SEQ ID NO: 6 (see pg. 60-80). However, the specification lacks a description for any isolated nucleic acid molecule which encodes

any *Homo sapien* polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2, wherein the polypeptide has one or more Tome-1 activities.

While Applicants' claim clearly recite a structure, (i.e. an isolated nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence having at least about 60% sequence homology to SEQ ID NO: 2), the specification, however, does not provide a disclosure of any particular structure to function/activity relationship between any isolated nucleic acid molecule and the encoded polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2. The specification also lacks description with respect to what function, if any, is required for any isolated nucleic acid molecule which encodes any polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2, wherein the polypeptide has one or more Tome-1 activities (see above 112 2nd paragraph rejection). Further, the specification fails to describe any isolated nucleic acid molecule which encodes any polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2, wherein the polypeptide has Tome-1 activities such as modulating wee1 ubiquitinylation, modulating wee1 degradation, modulating an SCF complex component activity and modulating mitotic activity. Given the lack of additional representatives of any isolated nucleic acid molecule which encodes any polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid

sequence consisting of SEQ ID NO: 2, wherein the polypeptide has one or more Tome-1 activities as encompassed by the claim, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 1-13 and 26 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, because the specification, while being enabling for an isolated nucleic acid molecule comprising a nucleotide sequence consisting of SEQ ID NO: 5, does not reasonably provide enablement for any isolated nucleic acid molecule which encodes any polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2, wherein the polypeptide has one or more Tome-1 activities. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to

practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Claims 1-13 and 26 are so broad as to encompass any isolated nucleic acid molecule which encodes any polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2, wherein the polypeptide has one or more Tome-1 activities.

The claims rejected under this section of U.S.C. 112, first paragraph, places minor structural limits on the "isolated nucleic acid molecule which encodes any polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2. Since the nucleic acid sequence encoding a peptide determines its structural and functional properties, predictability of which nucleic acid molecules can be used while obtaining the desired

function requires a knowledge of and guidance with regard to which nucleic acid molecules, if any, are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the nucleic acid molecules' structure relates to its desired function. In addition, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of different nucleic acid molecules encoding any polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2. The specification, however, only discloses a single nucleic acid molecule consisting of SEQ ID NO: 5 encoding a polypeptide consisting of SEQ ID NO: 2.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a nucleic acid sequence where modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility of the encoded protein are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass any nucleic acid molecule which encodes a polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2, wherein the polypeptide has one or more Tome-

1 activities because the specification does not establish: (A) regions of the nucleic acid molecule which may be modified without effecting the desired activity of the encoded protein; (B) the general tolerance of said nucleic acid molecules to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any nucleic acid molecules with an expectation of obtaining the desired biological function of the encoded protein; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Because of this lack of guidance, and the fact that the relationship between the polypeptide sequence of a protein and its activity/function are not well understood and unpredictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to make and practice any isolated nucleic acid molecule which encodes a polypeptide comprising any amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2, wherein the polypeptide has one or more Tome-1 activities.

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 5-13 and 26 are rejected under 35 U.S.C. § 102(b) as being anticipated by Walker et al. (WO/2002/018575).

The instant claims are drawn to an isolated nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2, wherein the polypeptide has one or more Tome-1 activities.

Walker et al. teach genes expressed in the cell cycle. Walker et al. specifically teach an isolated nucleic acid molecule (SEQ ID NO:3 of WO/2002/018575), which has 97% sequence homology to the Applicant's SEQ ID NO: 5, wherein the SEQ ID NO:3 of WO/2002/018575 encodes an amino acid sequence having at least 60% sequence homology to Applicant's SEQ ID NO: 2, wherein the SEQ ID NO:3 of WO/2002/018575 has one or more Tome-1 activities (see above 112 2nd paragraph rejection). Further, Walker et al. teach that CDC23, which is a protein encoded by the SEQ ID NO: 3 of WO/2002/018575, is a component of anaphase-promoting complex that regulates mitosis by catalyzing the formation of cyclin B-ubiquitin conjugates, targeting cyclinB for degradation (see pg. 19, lines 19-24), thereby anticipating "Tome-1" because it is also a protein that has a destruction box, F box, a KEN sequence or an activity that modulates mitotic entry (see 112 2nd paragraph rejection above). Therefore, Walker et al. anticipate Claims 1-3, 5 and 6.

Teachings of Walker et al. also anticipate the limitations of Claims 7, 8 and 26 because it is an inherent property of SEQ ID NO:3 of WO/2002/018575, which is 97% homologous to the Applicant's SEQ ID NO: 5, to hybridize to and be complementary to

the Applicant's SEQ ID NO: 5. Walker et al. further teach the hybridization conditions and methods using the cDNAs of the Sequence Listing as disclosed on pg. 24-27 under section heading "VIII Hybridization Technologies and Analyses. Walker et al. also teach complementary molecules to the cDNA for use in detection and inhibition of gene expression on pg. 27-28 under section heading "IX Complementary Molecules."

Walker et al. teach the protein expression of the cDNA in their Sequence Listing using pUB6/V5-His vector in either CHO cells for mammalian expression or Sf9 cells for insect cell expression (see pg. 28 under section heading "X Protein Expression). The expressed proteins cloned in pUB6/V5-His expression vectors comprise affinity tags consisting of V5 epitope and His_6, making the expressed proteins a heterologous protein. Therefore, Walker et al. anticipate Claims 9-13.

Therefore, Walker et al. anticipate the Applicants' isolated nucleic acid molecule which encodes a polypeptide comprising an amino acid sequence having at least about 60% sequence homology to an amino acid sequence consisting of SEQ ID NO: 2, wherein the polypeptide has one or more Tome-1 activities.

Conclusion

Claims 1-13 and 26 are rejected for the reasons as stated above. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

The instant Office action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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